

## REMARKS

Claims 1-4 and 32-36 are in this case. Claims 32-36 have been added. Support for claims 32-36 is found in Table I on page 6 of the application.

The first paragraph on page 1 of the specification has been amended to insert VIP after vasoactive intestinal peptide, insert SOM after somatostatin, insert BOM after bombesin and correct the spelling of bombesin.

The paragraph bridging pages 2 and 3 has been amended to insert Methyl leucine.

Marked-up pages of these paragraphs are attached.

Dxg is defined at page 3, line 3. Dxg is a general abbreviation of  $\alpha,\alpha$ -dialkylated glycines. Examples of Dxg amino acids are listed on page 3, lines 5 and 6. Aib is defined at page 3, lines 6-7.

Applicants consider that the abbreviations are clearly defined and therefore it is respectfully requested that the objection to the specification be withdrawn.

The Examiner has rejected claims 1-4 under 35 USC 112, first paragraph. Applicants respectfully traverse this rejection.

Claims 1-2 are directed to peptides. Although the peptides can be used to treat cancer this use is not claimed in claims 1 and 2. Therefore, as to claims 1-2 it is respectfully requested that this rejection be withdrawn.

As to claims 3 and 4, applicants draw the Examiner's attention to example 1 of the specification. It is well known in the cancer art that the National Cancer Institute has established an *in-vitro* screening protocol that utilizes up to 60 cell lines. One of the first steps in identifying clinical candidates for cancer treatment is to screen the drug against a series of carcinogenic cell

lines. One test that is used is cytotoxicity against the cell line. Based on these results a drug may be selected for further testing including *in -vivo* testing in small animals.

As explained on page 5, the cytotoxic activity of the peptides were tested on 8 human tumor cell lines. These tumor cell lines are standard cell lines that are used to test candidate substances. This is an art recognized model. This data would enable one skilled in the art to make and use the invention of claims 3 and 4 and newly added claims 32-36.

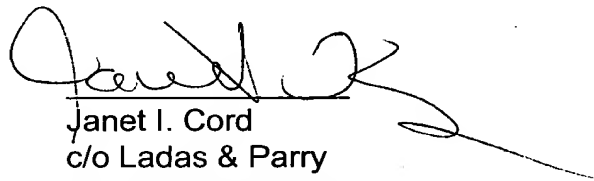
Therefore it is respectfully requested that this rejection be withdrawn.

The Examiner has rejected claims 1-4 under 35 USC 112, second paragraph. Applicants respectfully traverse this rejection. Dxg and Aib are defined in the specification.

Therefore it is respectfully requested that this rejection be withdrawn.

Applicants submit that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,



Janet I. Cord  
c/o Ladas & Parry  
26 West 61st Street  
New York, New York 10023  
Reg. No. 33,778 (212) 708-1935

This invention relates to novel peptide analogs of vasoactive intestinal peptide (VIP), somatostatin (SOM), bombesin [bombesin] (BOM) and Substance P. This invention also relates to the use of the novel peptide analogs for the treatment of cancer.

The VIP receptor binding inhibitor VIP<sub>2</sub> (Leu-Met-Tyr-Pro-Thr-Tyr-Leu-Lys) (SEQ ID NO:1) has been shown in our previous studies to be a selective cytotoxic peptide for cancer cells having receptors for vasoactive intestinal peptide. Novel peptides that have conformational constraints and resist enzymatic degradation are formed by replacing any of the amino acids of the sequence Leu-Met-Tyr-Pro-Thr-Tyr-Leu-Lys with D<sub>xg</sub>. D<sub>xg</sub> represents cyclic and acyclic dialkylated glycines where the cyclic ring is a C<sub>3</sub>-C<sub>8</sub> ring and the number of carbon atoms in the alkyl group is from 1 to 6 (methyl to hexyl). Examples are Aib, MeLeu (methyl leucine), Di-ethylglycine and its higher homologs, and 1-amino cycloalkane carboxylic acids. Aib represents  $\alpha$ -amino-isobutyric acid.